

SCIENCE

FRIDAY, JULY 28, 1944

No. 2587

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SCIENCE: A Weekly Journal devoted to the Advancement of Science. Editorial communications should be sent to the editors of SCIENCE, Lancaster, Pa. Published every Friday by

THE SCIENCE PRESS

Lancaster, Pennsylvania

Annual Subscription, \$6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington 25, D. C.

ADVENTURES IN BIOLOGICAL ENGINEERING¹

By Dr. HUDSON HOAGLAND

EXECUTIVE DIRECTOR OF THE WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY AND FELLOW OF THE JOHN SIMON GUGGENHEIM MEMORIAL FOUNDATION

MAN, together with other higher vertebrates, has developed some elegant automatic mechanisms for regulating the physical and chemical properties of his blood and body fluids. The relative constancy of one's internal environment in the face of external stress and change is characteristic of such factors as blood volume, blood sugar, hydrogen ion concentration and salt content of the body fluids. The thermodynamic regulation of internal body temperature is another case in point. These factors are beautifully controlled with little or no conscious thought on our part. As Claude Bernard pointed out nearly a century ago this regulation renders the higher vertebrates free of their external environment to a degree impossible for animals not possessing these automatic mechanisms. Homeostasis of the internal environment, as

Cannon, Barcroft and others have demonstrated, is one of the truly central problems of physiology.

When, for example, the environmental temperature falls a bird or mammal conserves more of its metabolic heat and maintains its internal temperature constant. A frog, on the other hand, must take on the temperature of its environment. In cold weather its metabolism and other dependent reactions are slowed until it becomes immobilized and a prisoner of the climate. Freedom thus is not just a matter of sociology and politics, but freedom of a sort has its substratum in biochemistry and physiology.

In recent years with the development of aviation man has desired to be free in an environment for which his evolutionary history could not possibly have fitted him. In high-speed airplanes he is assailed by new and formidable stresses. Living as he does at the bottom of a sea of air supplying a continuous and

¹ Sigma Xi initiation lecture given at Worcester Polytechnic Institute on June 14, 1944.

plentiful amount of oxygen he has been unprepared by evolution to store oxygen in his body as he has been able to store water and foodstuffs that come to him only at intervals. He therefore must carry his oxygen supply with him when he flies to high altitudes. He must also adjust to severe and unaccustomed accelerations and rapid changes of atmospheric pressures which, together with the peculiar emotional stresses of modern aviation, may be exacting in the extreme. Since we can not wait for evolution to prepare us to cope with this new environment it is the primary task of aviation medicine to devise means of preventing the stresses of flight from interfering too greatly with our homeostatic mechanisms.

This evening I should like to consider how some of the stresses of flying and of flight type operations may be reflected in the urinary excretion of hormones from the adrenal cortex and how the administration of certain hormones and hormone type substances may affect performance in fatiguing psychomotor tasks encountered not only in aviation but also in industry.

We shall not be concerned with problems involving the adrenal medulla. Thanks to intensive work over the past forty years the role of adrenin or epinephrin, the hormone from the adrenal medulla, is well understood. Physiologists and biochemists in recent years have only begun to understand the more complicated story of the adrenal cortex. Despite the fact that cortex and medulla are parts of the same small gland the functions of these structures are very different and the types of hormones they synthesize belong to chemically quite distinct families.

Some twenty hormones have been extracted from the adrenal cortex. They all belong to the class of substances known as steroids—four carbon ring structures with relatively simple side chains, and with molecular weights of around 300. The sexual apparatus, testes, ovaries, corpus luteum and placenta also manufacture and secrete a variety of steroids differing only in minor structural details from each other and from the hormones of the adrenal cortex. For example, slight differences only in molecular configuration differentiate the oestrogens which regulate the sexual cycle of the female from the male sex hormones of the testes and from the steroids of the adrenal cortex concerned with essential life maintaining processes such as salt and water balance and aspects of sugar storage and metabolism. The situation is not clarified by the finding that a few of the same steroids are manufactured and released both by the sexual apparatus and, to a lesser degree, by the adrenal cortex as well.

Steroids are excreted in the urine primarily in the form of 17-ketosteroids, that is as steroids with an oxygen atom attached to a particular carbon in one of

the rings. There are 17 carbon atoms in the four ring steroid skeleton and the oxygen or keto radical is on the conventionally numbered 17th carbon atom. The 17-ketosteroids are thus end products of steroid hormone metabolism and, for the most part, are hormonally inactive. It is believed that the 17-ketosteroids come primarily from adrenal cortical chemical precursors rather than from precursors of the gonads because (a) in Addison's disease in which the adrenal cortex becomes non-functional there is a decline in the output of 17-ketosteroids corresponding to the severity of the disease, (b) in certain cancerous growths of the adrenal cortex there is a marked overpouring of 17-ketosteroids, (c) in ovariectomized women with healthy adrenals the output is normal and (d) in castrated males the output is 80 to 90 per cent. of normal.² The average output per 24 hours for healthy normal men is 7 to 27 mg and for women 5 to 16 mg. The 17-ketosteroids are extracted from the urine by organic solvents and are finally quantitatively determined with a spectrum photometer.

Available evidence indicates that hormones of the adrenal cortex play a significant role when the organism encounters stressful situations. Animals forced to severe exercise, or exposed to very low oxygen tensions or extremes of cold first display a hyperplasia of the cells of the adrenal cortex followed later by atrophy. It has been well established that adrenalectomized animals early show marked weakness and lassitude preceding collapse and death, and that they do not withstand stressful situations. The syndrome of Addison's disease in man is typically characterized by lassitude and exhaustion. Adrenalectomized animals and Addisonian patients can be maintained in a healthy state by adrenal cortex hormones.

As a result of association with a group of navy instructor pilots in the summer of 1940 I became impressed with the fatiguing character of their work. Flight instruction of 90 hours per month was very tiring for some men. As a result of discussion of this matter with my colleague, Dr. Gregory Pineus, he suggested the possibility that adrenal cortical function might be related to this type of fatigue and that hormone medication might prove of value in combating it. We accordingly decided to investigate the matter.

Our first task was to determine the output of urinary 17-ketosteroids at intervals during the day in normal

² For citations to these matters and to other points discussed in this lecture the reader is referred to G. Pineus and H. Hoagland, *Jour. of Aviation Med.*, 14: 173, 1943; and G. Pineus and H. Hoagland, *Jour. of Aviation Med.*, 15: 98, 1944. These two papers present the data of the fatigue studies described below with the exception of our as yet unpublished studies of industrial fatigue.

³ Laboratory director of the Worcester Foundation for Experimental Biology.

the first healthy young men going about their daily, and not especially stressful, routine. Modifications, made in our laboratory, of standard procedures rendered it possible to make reliable 17-ketosteroid determinations on samples of urine, as small as typical one-hour collections. We accordingly made 97 determinations over a period of days on seven men working in our laboratory. While much individual variation in levels of output were encountered we were at once struck with the fact that sleep excretions were low and rose on an average of 60 per cent. in the hours immediately after waking, falling in an essentially linear fashion during the course of the day and reaching minimal levels again at night. This diurnal rhythm was a true sleep-waking rhythm since a reversal of night and day activities reversed the rhythm. It was as if the process of waking and starting the day itself produced a stress response of considerable magnitude from the adrenal cortex.

Since aviation personnel was not at first available we next proceeded to study a group of male Clark University student subjects in our own laboratory, who were subjected to the fatiguing operations of a pursuit meter. In our early series of tests we used an apparatus designed by Dr. Smith Stevens, of Harvard University, consisting of airplane type controls that moved a bar of light over prescribed pathways across a photosensitive screen. Errors were recorded automatically when the light strayed off the pathways. Continuous operation of this apparatus for two or three hours was very fatiguing and with skilled operators, *i.e.*, those having had 10 to 15 hours of practice, the score of errors increased measurably in the second halves of the tests.

Carefully timed control urine samples were collected covering at least a two hour period just before each run, and experimental samples were taken immediately after the fatiguing bout which lasted from two to six hours. Since we had observed that time of day has an effect on the relative excretion level of 17-ketosteroids we corrected each control from our standard curve to make it correspond to the time of day of the experimental sample. In this way arithmetic differences between "flight" and control samples in terms of mg ketosteroids per unit of time could be compared for a given test. We were interested to see that the fatiguing bout considerably augmented the output of 17-ketosteroids. The increased output under stress after subtracting the control values corrected for time of day to coincide with the time of the experiment we shall hereafter refer to as stress 17-ketosteroids.

Sixty-nine test runs on seven men brought out some rather striking results when we plotted each man's mean stress 17-ketosteroids against his error scores

for the second halves of his test. Each individual displayed a characteristic performance level and a corresponding level of output of stress 17-ketosteroids. The men turning up the best performances showed little increase in output of 17-ketosteroids over their control values, while those showing high error scores in the second halves of the tests yielded consistently a high output of stress 17-ketosteroids. The urinary steroids were, in short, an index of scoring ability in long runs on the Stevens apparatus especially in the second halves of fatiguing bouts. The men best conserving their steroids were the best performers.

In addition we found a marked increase in urine volume excreted per unit time during the tests as compared to controls and with somewhat less regularity this augmented diuresis paralleled poorness of performance. Not only did these relationships hold between men, *i.e.*, the poorer performers excreting more 17-ketosteroids and also more urine but it held within men, *i.e.*, the individual tended to score best when his "flight" increase in urine volume or stress 17-ketosteroid level is least. For stress 17-ketosteroids as against all scores the correlation coefficient, r , was 0.723. It was 0.519 for diuresis and all scores. For scores *within* men these values were respectively $r = 0.686$ and 0.530 . All four correlations were significant with P values of < 0.01 . This urinary stress effect is apparently quite general since we have found it with a variety of stressful situations some of which will be described in detail later. For example, urine samples were obtained on five university students just before and just after they undertook final or doctoral examinations lasting from one to three hours. The 17-ketosteroid output and urine volume excreted per unit time was raised by the stress of the examinations as compared to the control samples.

What is the relationship between the enhanced water and steroid output? Is the increase in urine volume under stress due to enhanced formation of metabolic water as a by-product of increased muscle tone which then merely washes out more steroid material? This is evidently not the case. Pincus⁴ has shown that excessive water intake with resulting marked diuresis does not increase the output of 17-ketosteroids and this finding has been confirmed by others. In fact, our evidence indicates that the enhanced hormone excretion from stress precedes, if anything, the diuresis. Presumably hormones from the adrenal cortex, some of which are known to be concerned with water and electrolyte balance, bring about the enhanced water excretion, although it is possible that both effects are by-products of some as yet unknown mechanism perhaps involving the direct

⁴ G. Pincus, *Jour. Clin. Endocrinol.*, 3: 195, 1943.

action of pituitary hormones under nervous control by the hypothalamus.

The Stevens serial coordination meter originally designed for other purposes was not altogether satisfactory for our needs and accordingly Dr. Nicholas Werthessen, Mr. Murray Edinburgh and I designed and built an apparatus which better approximates certain aspects of flight. This apparatus consists of airplane stick and rudder pedal controls that operate a pointing rectangular light beam. At approximately eight feet in front of the operator an airplane model mounted on the end of a rod is caused to move in a thoroughly random and nonrepeating fashion, banking to left and right and moving up and down. In the two "engine nacelles" of the model are photoelectric cells. The operator must "fly in tight formation" with this model by simultaneously bracketting both photoelectric cells with his rectangular beam of light. He is automatically scored for his ability to do this; a counter registers each time he slips off one or both cells with his pointing light and clocks register his per cent. time on target for any chosen interval. In this way, for example, by taking five minute readings over a continuous run of an hour a curve of performance can be plotted characteristic of the individual. For practiced operators these curves show a decline characteristic of the individual during the test. A single numerical measure of fatigue can be had by dividing the mean score for the first half of a run into that for the second half. Thus, a fall of this ratio below unity for a skilled operator is a measure of his fatiguing. For most people seven to ten hours of practice are needed before the learning curve is flat although, because of "transfer of learning," professional aviators usually show flat learning curves in two to three hours. Army pilots who have used this apparatus say it is about as fatiguing as close formation flying under poor weather conditions.

Since responses to anoxia are of interest in aviation our first use of the target meter was to observe the effects of breathing mixtures of air containing reduced amounts of oxygen on scoring ability and on the excretion of 17-ketosteroids. Twenty-seven experiments were carried out on three young men in a gas chamber at the Harvard Fatigue Laboratory after they had completed a series of learning runs. Oxygen mixtures, at sea-level pressures, from 21 to 13 per cent. were used and CO_2 was absorbed by soda lime. This lower value of 13 per cent. oxygen corresponds to an altitude of about 14,000 feet in terms of oxygen saturation of the blood hemoglobin. The results were interesting in that measurable decline in performance curves were seen at oxygen levels corresponding to altitudes as low as 8,000 feet and became progressively more accentuated at lower oxygen percentages.

With declining performance at decreasing oxygen tensions the stress 17-ketosteroid output rose steeply, and did the excessive output of urine. The combined stresses of low oxygen and target meter performance evidently called strongly on adrenal cortical reserves.

At about this time we were fortunate to be invited to make a study of a volunteer group of Army instructor pilots at a southern air training center. The measurement of the stress of flight was at first a source of much puzzlement but an ingenious suggestion of Dr. Pineus enabled us to measure quantitatively the effects of flight stress on 17-ketosteroid output. The method was as follows: Each pilot before putting on his flying clothes emptied his bladder and accurately recorded the time of voiding. At the end of the period of flying, on his return to the locker room, he urinated into a bottle and again recorded the time. In addition he also recorded the actual duration of time spent in the air. Thus for any flight lasting from one to four hours we obtained a urine specimen which had collected in the pilot's bladder not only during the time spent in the air but also during time on the ground just prior to the take-off and for the period after landing while the machine was being brought to the line and the pilot was checking in, returning to the locker room and changing clothes. There was considerable variation in the percentage of time a pilot was actually air-borne. Some flew only 30 per cent. of the time over which the sample collected while others were in the air as much as 95 per cent. of the time. From the data the percentage of total time that the pilot was actually air-borne could be calculated. In addition for each of these flight samples the pilot furnished on the same day, a separate timed control specimen of his urine. Data were thus obtained from 16 pilots for 152 flights and control samples and a plot was made of the stress 17-ketosteroids against the percentage of the time the pilot was air-borne for each flight. The results were interesting—a linear relationship was obtained between per cent. increase in stress 17-ketosteroids and per cent. of time in the air such that the greater the time in the air the greater was the steroid output. The correlation was $r = 0.978$, < 0.01 . A repetition of this experiment carried out by us on seven Pratt & Whitney test pilots during 8 flights gave a similar result. In this series r equalled $0.922 \pm < 0.01$.

From our laboratory experiments we had noted a positive relationship between tendency to fatigue, i.e., to score badly in the latter part of tests and the excretion of stress 17-ketosteroids. We accordingly asked the commanding officer to grade the sixteen pilots of his squadron who were our experimental subjects in terms of his opinion as to their fatigability putting the least fatigable man at the top of his list. The pilot

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ere teaching flight some 90 hours per month and ere well known personally to their commander from onths of association. We, in turn, rated these men tirely from their urine data putting the lowest ex- eter of stress 17-ketosteroids at the top of the list. n matching the two rating tables we were impressed ith the correspondence. Our numbers 1, 13, 14, 15 d 16 men agreed on both listings. There were many serepancies for men in between but with, none the ss, a tendency to agreement as indicated by a corre- tion coefficient of 0.676 with a P value of < 0.01 etween our urinary index and the commander's sub- jective evaluation of his men's ability "to take it."

From what has been said it appears that marked variations in the abilities of men to withstand fatig- ing ordeals is related to their adrenal cortical func- tions and it was natural to ask if the administration of suitable steroids might increase one's ability to withstand the type of measurable stress we were inves- tigating. We have accordingly tested several steroid substances and have found one in particular, Δ^5 preg- nenolone, a synthetic compound supplied to us by the Schering Corporation, that has improved and pro- longed scoring ability on our pursuitmeters without having any deleterious after effects. We have com- pared the action of this substance to that of placebo pills that look and taste just like it but which contain no active principle. From 356 experiments on 21 healthy young men we have found, in most cases, marked improvement in target meter performance when they orally took 50 mg per day of pregneno- lone.⁵ In addition, comparable experiments on a group of over 100 volunteer industrial workers in two industrial war industries engaged in a variety of operations involving incentive piece work pay have shown statistically significant improvement in pro- duction rates and in waste saving when taking preg- nenolone as contrasted to placebos (unpublished).

Objectively measured antifatigue effects of preg- nenolone are variable from person to person. Some show no improvement and report no subjective symp- toms from its use but a substantial number have re- ported feeling less fatigued and better able to cope

with their jobs when they were taking it as contrasted to periods when they were taking placebos. That pregnenolone when given orally is absorbed and trans- formed in the body into a variety of hormonally active steroid substances has been demonstrated in our lab- oratory (unpublished). From urine analyses of avia- tors who took pregnenolone during actual flight tests their curve of percent time in air vs. stress 17-keto- steroids rises at only approximately half the rate of the curve when not on pregnenolone. This we believe indicates a sparing action of hormone secretion on the adrenal cortex when pregnenolone is administered. But just how or why this substance should alleviate fatigue remains for future investigations to demon- strate.

Other steroids may prove to be as efficacious in counteracting psychomotor fatigue as is pregnenolone. We obtained negative results with adrenal cortical ex- tract and progesterone in a series of tests, but these do not rule out the possibility that these substances may counteract fatigue since the amounts we used in our preliminary tests and the number of our ex- periments may have been inadequate to show possible effects.

We are convinced that pregnenolone is most effec- tive in combatting fatigue where motivation is high and where men are working under really trying con- ditions. Our hard worked pilots who were profession- ally interested in making high scores on the target meter showed more improvement on pregnenolone (average 25 per cent.) than did our paid civilian sub- jects (average 10 per cent.) who were not under as much working stress and whose interest in the experi- ments was less. In a third industrial group that we investigated in which there was no incentive pay preg- nenolone did not increase production over placebo levels.

We believe that these findings to date are of a pre- liminary nature. The increase of human working efficiency without evidence of artificial overstimulation and untoward side effects is a desirable objective. We hope that others will be able to confirm us and advance this aspect of the field of biological engi- neering.

OBITUARY

HARRY FIELDING REID

DR. HARRY FIELDING REID, emeritus professor of dynamical geology and geography of the Johns Hop- kins University, died on Sunday, June 18, just one month after his 85th birthday. Born in Baltimore, he took his A.B. and Ph.D. degrees at the Hopkins.

⁵ G. Pineus and H. Hoagland, *Jour. Aviation Med.*, 15: 8, 1944.

After graduation he served successively as professor of mathematics and then of physics at Case School, returning to his alma mater in 1894 as lecturer, then as professor of geological physics, retiring in 1929.

His was a long and distinguished career as a scien- tist as evinced by his early election to the National Academy of Sciences. He was devoted to the precise thinking and rigid demands of proof which doubtless

grew out of his mathematical training and exercised a very salutary influence by both example and precept in the field of geology which is, to such a large degree, an eclectic science. Early in his career he devoted much time to the study of glaciers, his investigations taking him to the Swiss Alps and on several trips to Alaska, where he discovered and named several glaciers as the Gilman and Johns Hopkins. Several valuable papers on the measurement and movement resulted. Dr. Reid was president of the Seismological Society of America from 1912 to 1914 and of the Geophysical Union from 1924 to 1926. For many years until the university moved to Homewood he ran the seismograph at the Hopkins, serving on many important committees of the Seismological Society and serving as special expert of earthquake records for the U. S. Geological Survey. He was appointed by President Wilson a member of the committee to investigate the slides that were so bothersome in the construction of the Panama Canal and a few years afterward to a second distinguished committee to study the great California earthquake that originated along the San Andreas fault. During the latter study Dr. Reid developed the slip theory of the origin of earthquakes. He was interested in all the aspects of dynamical geology, publishing fundamental papers on the mechanics of faulting. He was a consistent critic of the planetesimal hypothesis and of the many phases of orogenies and contributed much to establishing the dictum that the folding of rock masses is merely an early step in the formation of mountains which are primarily due to epeirogenic forces and erosion.

Dr. Reid was Hitchcock lecturer at the University of California in 1911. Along with the late Dr. Joseph S. Ames he was sent abroad by Woodrow Wilson to report on the war effort of British science in World War I. He was a member of many learned societies at home and abroad, including the International Geodetic and Geophysical Union, the American Philosophical Society, Geological Society of America, Academies of Sciences of Washington and Philadelphia, Société Helvétique des Sciences Naturelles, International Seismological Association, etc.

In 1898 when the Maryland Geological Survey inaugurated the good roads movement in Maryland, Dr. Reid served as chief of the highway division of the survey for seven years.

He was a life-long Democrat until the advent of the New Deal, a close friend of Woodrow Wilson and took a lively interest in Baltimore affairs. Personally he was rather reserved; consequently those who held him in high and affectionate regard were distinguished by their quality rather than their quantity. We, who were closely associated with him for so many years,

are happy to remember him as a very great gentleman and scholar.

Survivors are his widow, the author of intimate biographies of Dr. William Osler and Woodrow Wilson, a son Francis and a daughter Doris.

EDWARD W. BERRY

DAYTON STONER

SEIZED by an almost fatal heart attack in April, 1943, Dr. Stoner, after great apparent improvement and on a day when his cheerful disposition had been especially manifest, died of coronary occlusion on May 8, 1944. Funeral services were held at both his latest, and an earlier, home-town—Albany, N. Y., and Iowa City, Iowa, respectively—and interment was at North Liberty, Iowa, his boyhood home. He is survived by his wife, whom he married as Lillian R. Christianson at Iowa City in 1912, and by a sister, Miss Nellie D. Stoner, of Denver, Colorado.

Stoner was born on November 26, 1883, son of Marcus and Nancy (Koser) Stoner. From the public schools he went to the University of Iowa where as a student and member of the faculty he remained until 1928. He took the degrees: A.B. in 1907, M.S. in 1909 and Ph.D. in 1919. Beginning as instructor in zoology the year after graduation, he advanced to the grade of assistant professor. About 1912 he engaged in summer studies of insect biology and control for the State College of Iowa. The summer of 1916 was taken up by teaching at the Okoboji Lakeside Laboratory of the University of Iowa and those of 1919 and 1920 at the Douglas Lake Biological Station of the University of Michigan. He was a field assistant in the Federal Bureau of Entomology from 1928 to 1931, during which years he also had summer employment as a field ornithologist for the Roosevelt Wildlife Station in New York. From 1932 until his death, he was state zoologist of the New York State Museum. He was an affiliate of the American Association for the Advancement of Science, American Society of Mammalogists (charter member), American Ornithologists' Union (member class), National Audubon Society, Wildlife Society, Wilson Ornithological Club, Northeastern Bird Banding Association, Iowa Academy of Sciences (fellow), Iowa Ornithologists' Union and Sigma Xi.

Stoner was fortunate in accompanying the Iowa State College expedition to Vancouver Island in 1913, and those of the University of Iowa to Barbados and Antigua in 1918, and Fiji and New Zealand in 1922. Some ten to twelve of his papers reported on traveling and collecting experiences on these trips. His interests in the earlier years of his publishing career tended to center about insects and in the later ones

upon birds. Among insects, the Pentatomoidea, claiming most of his attention, were the subject of sixteen publications, the largest of which on "The Scutelleridae of Iowa" (1920) ran to 140 pages. This was his doctor's thesis. His entomological collections are to be presented to the United States National Museum. His published ornithological writings number nearly hundred. Of these, sixteen relate to the bank swallow, a species he studied more thoroughly than has any other investigator. In the course of this work he became especially interested in the body temperature and growth of birds. His studies in those directions were later extended to the house wren, barn swallow, cliff swallow and phoebe. The modern technic of banding was applied in these studies as well as in other investigations carried on in Michigan and Iowa. The University of Iowa Service Bulletins he prepared, entitled "Bird Migration," "Spring Birds," "Winter Birds," "Planting for the Birds" and "Summer Birds of Iowa," were reprinted from time to time to supply the demand. In number of pages (nearly 500), the "Ornithology of the Oneida Lake Region" surpassed any other of his papers on birds.

Mammals received a due share of attention, being the subject of eight published contributions of which "The Rodents of Iowa" (172 pp., 1918) was used as reference, almost as a text-book, in several colleges and universities of the upper Mississippi Valley. From this recital it is evident, despite the assertion that there no longer are any old-fashioned naturalists, that Stoner must be given that rank. In addition to writing in the fields thus far noted, he was a pioneer in recording and commenting on the toll of the automobile among wildlife, the first of his ten articles on that subject appearing in 1925. He wrote also on reptiles, amphibians, *Craspedacusta*, *Peripatus* and the black widow spider. Two biographical sketches from his pen related to John J. Audubon and Charles C. Nutting. A number of manuscripts, mostly on birds, are complete and it is to be hoped will be published.

The study upon which Stoner was engaged for the U. S. Bureau of Entomology was that of the natural enemies of the leaf-tyer and other insect pests of celery. A comprehensive manuscript upon the subject is on file in Washington with the organization named. A summary of the section relating to "Reptiles and Amphibians in Relation to Celery Insects in the Sanford Florida District" was published in 1937 and another on birds was prepared for publication by the U. S. Fish and Wildlife Service, in whose files it still reposes.

Although he left the teaching field, Stoner remained a teacher as shown by his reports as state zoologist and by the interest he took in the *Bird Day Bulletin*

to the schools in New York. Each year, besides contributing to this bulletin himself, he wrote many letters soliciting articles from others that would keep the publication of state-wide pertinence and interest. Often the essays received had to be rewritten to meet the pedagogical requirements of the bulletin. This work he continued for twelve years.

Stoner was systematic and conscientious in his work and conservative in reaching conclusions. He was always optimistic and pleasant and leaves a memory that will be treasured by his friends.

W. L. McATEE

WILDLIFE SERVICE,
CHICAGO

RECENT DEATHS

DR. PHILIP FOX, astronomer, colonel in the Signal Corps of the U. S. Army, from 1937 to 1940 director of the Museum of Science and Industry, Chicago, later head of the Army Electronics Training Center at Harvard University, died on July 21 at the age of sixty-six years.

DR. HERBERT HARVEY KIMBALL, from 1927 to 1932 senior meteorologist of the U. S. Weather Bureau, from 1932 to 1939 research associate in charge of solar radiation investigations at the Blue Hill Observatory of Harvard University, died on July 15. He was eighty-two years old.

DR. EDWARD LUTHER STEVENSON, historian and geographer, who was professor of history at Rutgers University from 1891 to 1911, died on July 16 at the age of eighty-five years.

DR. ALFRED P. LOTHROP, professor of organic chemistry at Oberlin College, died on July 6 at the age of sixty years.

ALEXANDER WATTS MCCOY, consulting petroleum geologist, died on June 30 at the age of fifty-five years.

STANLEY SEARLES, SR., for many years, until his retirement in 1939, editor for the Bureau of American Ethnology, died on June 23, at the age of seventy-six years.

DR. ARTHUR HENRY REGINALD BULLER, F.R.S., professor of botany emeritus of the University of Manitoba, died on June 30. He was in his seventieth year.

A CORRESPONDENT writes: "The great Canadian botanist, Frère Marie-Victorin, director of the Botanical Institute of the University of Montreal and founder of the Montreal Botanical Garden, was killed in an automobile accident on the night of July 15, near St. Hyacinthe, Que., while returning from a botanical trip at Black Lake, Megantic County. He was fifty-nine years old."

SCIENTIFIC EVENTS

THE BENGAL FAMINE

IN regard to the recent famine in Bengal, India, Dr. A. V. Hill writes to *The Times*, London, as follows:

There has been much fruitless recrimination about the recent famine in Bengal: instead of arguing about the symptoms, let us face the facts of the disease itself.

(1) The mortality in India at all ages is four to eight times ours; the expectation of life at birth is 26 years instead of our 62; only half the people born reach 22 years, instead of 69 with us.

(2) Ill-health is correspondingly prevalent; between 100 and 200 million people, out of 400 millions, suffer from malaria every year; tuberculosis, cholera, small-pox, plague, guinea-worm and filarial infection, yaws, kala-azar and many other diseases take their continual toll of life and health.

(3) A large part of the population is underfed, according to any reasonable standards more than half; of these, many millions are living near the verge of starvation.

(4) Chronic malnutrition acts with disease in a vicious circle, producing poverty and inefficiency.

(5) In spite of all this, the population of India is increasing now by about 6,000,000 a year, about 15 per thousand per annum.

There is nothing new about disease and under-nourishment in India: indeed the present population trend is a sign that they have rather less effect than formerly. . . . Already about 50 per cent. more food is needed in India. Can agriculture by present methods catch up and cope with the expanding population?

It is idle to talk of family limitation, except as a long-term policy; and the present need is acute. The factor of safety indeed in India is very low. Disorganization or disorder could lead to frightful tragedy. Cooperation by all men of good will in the whole-hearted development of India's resources by modern scientific methods is the only hope of averting it.

THE FORESTRY MISSION TO CHILE

THE technical forestry mission sent to Chile by the Forest Service of the U. S. Department of Agriculture at the request of the Department of State has now completed its work in Chile and has returned to the United States to prepare a formal report. This mission consisted of five technicians: I. T. Haig, assistant chief of the Division of Forest Management and Research, in charge; Lawrence V. Teesdale, Forest Products Laboratory, wood utilization specialist; Philip A. Briegleb, Pacific Northwest Forest Experiment Station, in charge of timber surveys; Burnett H. Payne, North Pacific Region, evaluation surveys, and Martin A. Haertel, specialist in hardwood chemical distillation.

This project, initiated at the request of the Corpora-

cion de Fomento de la Producción, an agency of the Chilean Government, had as its objective an appraisal of the forest resources of Chile and its evaluation as a basis for the expansion of forest industries. This is part of a broad scale program to industrialize the country in so far as natural resources permit and to help to stabilize Chilean economy.

The mission spent six months in a rapid appraisal of the forest situation, including a study of forest volume, distribution and economic availability, forest depletion, forest growth and national timber requirements both present and future. Highlights of the forest situation are: (1) Chile has a substantial forest area; on a *per capita* basis her commercial forest acreage is fairly comparable with that of the United States. (2) There is no forest practice worthy of the name in the natural forest area, even organized fire protection being entirely lacking. In contrast, the small but substantial plantation area is very intensively managed; stand improvement operations beginning in some types at as early as four years of age with harvest cutting frequently at twelve to fifteen years of age. (3) Under crude forestry, primarily fire protection, the forest resources could sustain on a permanent basis two to three times the industry now based upon it.

THE NEW YORK CITY MEETING OF THE AMERICAN CHEMICAL SOCIETY

THE one hundred and eighth meeting of the American Chemical Society will be held in New York City from September 11 to 15, under the auspices of the North Jersey Section, which has two thousand three hundred and thirty-two members, with headquarters in Newark. The meeting will be devoted to wartime research, problems of the chemical industry and post-war activities of the profession. It is expected that there will be meetings of all divisions except the Division of the History of Chemistry. More than a hundred local sections of the society will be represented.

Rubber, petroleum, food, plastics, fertilizer, cellulose, gas and fuel, medicinal chemistry and education are among the general fields of discussion. Catalysis will be the chief subject discussed by the Petroleum Division, which will also hold a round table on bench scale techniques in addition to general sessions. The chairman of this section is Dr. Cecil L. Brown, of the Standard Oil Company of Louisiana. Cellulose and cellulose plastics will be discussed at joint sessions of the Cellulose, Colloid, Physical and Inorganic Divisions.

The American Chemical Society is the largest professional organization of its kind in the world with a membership approaching forty thousand. It has

hundred and four local sections located in all parts of the country.

CIVILIAN MEDICAL CONSULTANTS OF THE ARMY MEDICAL DEPARTMENT

THE War Department announced on June 5 the appointment of nineteen civilian physicians as advisers to the Army Medical Department on problems of internal medicine. The advice of these consultants will supplement that afforded by the special consultants selected from officers in the Medical Corps of the Army and will be carried on through the chief consultant of the department of medicine, Brigadier General Hugh J. Morgan. The consultants appointed, in eight special fields of internal medicine, are:

Dr. Robert Cooke, assistant professor of clinical medicine, Cornell University (allergy).

Dr. Francis Rackemann, physician, Massachusetts General Hospital, Boston (allergy).

Dr. Robert Levy, professor of clinical medicine, College of Physicians and Surgeons, Columbia University (cardiovascular disease).

Dr. Paul White, chief of Cardiac Clinics and Laboratory, Massachusetts General Hospital, Boston (cardiovascular diseases).

Dr. Chester Keefer, professor of medicine, Boston University School of Medicine (chemotherapy).

Dr. Chester Jones, clinical professor of medicine, Harvard Medical School (gastro-enterology).

Dr. Walter L. Palmer, professor of medicine, School of Medicine, of the University of Chicago (gastro-enterology).

Dr. Colin MacLeod, professor of bacteriology, College of Medicine of New York University (infectious diseases).

Dr. Charles E. Smith, professor of public health and preventive medicine, School of Medicine, San Francisco, Stanford University (infectious diseases).

Dr. Carol B. Thomas, associate in medicine, the Johns Hopkins University (infectious diseases).

Dr. Barry Wood, professor of medicine, Washington University, St. Louis (infectious diseases).

Dr. J. Gardner Hopkins, professor of dermatology, College of Physicians and Surgeons, Columbia University (skin diseases).

Dr. John Stokes, director, Institute for Control of Syphilis, University of Pennsylvania (skin diseases).

Dr. Mark F. Boyd, director of the Station for Malaria Research, Tallahassee, Fla. (tropical diseases).

Dr. Harold W. Brown, professor of parasitology, Columbia University (tropical diseases).

Dr. James A. Shannon, assistant professor of medicine, New York University College of Medicine (tropical diseases).

Dr. Robert B. Watson, principal malariologist, Tennessee Valley Authority, Chattanooga (tropical diseases).

Dr. J. Burns Amberson, professor of medicine, College of Physicians and Surgeons, Columbia University (tuberculosis).

Dr. James J. Warning, professor of medicine, School of Medicine at Denver of the University of Colorado (tuberculosis).

THE WORK OF DR. GEORGE HARRISON SHULL

IN an address to the House of Representatives on May 15, the Honorable George A. Dondero called attention to the work of Dr. George Harrison Shull, professor emeritus of botany and genetics of Princeton University, in which he spoke in part as follows:

Dr. George Harrison Shull has contributed much toward the production of food and has made very important contributions to the Nation and perhaps the world in his creation and propagation of hybrid corn. He may be one of the unsung heroes of the Nation. He deserves a high place in the history of food production.

In recognizing hybrid vigor, as it was displayed to him in his corn-breeding cultures following crosses between his highly inbred related lines, and in devising a practical method or agricultural technique for obtaining and utilizing hybrid vigor to the utmost through the use of hybridized seed corn, he demonstrated with striking clarity how research in pure science may lead to results of tremendous practical value.

The procedure which he devised for the practical production of hybrid corn and which he presented in 1909 before the American Breeders Association is in all essentials the basis of methods now used in producing seed of crossed corn for planting upward of 50,000,000 acres of field corn and sweet corn annually in the United States, including almost all of the Iowa corn acreage. The superiority and dependability of hybrid corn is demonstrated most markedly under adverse growing conditions. The trends in corn growing indicate that hybrid corn may soon replace ordinary corn almost completely for planting our annual acreage of upward of 90,000,000 acres. We have reason to believe that general use of hybridized corn seed may enable a somewhat reduced national acreage to produce an annual crop upward of 1,000,000,000 bushels in excess of the best national yields we enjoyed before we had hybrid corn.

Dr. Shull has not profited a penny through devising the agricultural technique which is basic to hybrid corn production. He derives much comfort from the fact that his hybrid corn research has come to be recognized as a classic example of work in pure science which has led directly to economic results of tremendous importance and which has proved of incalculable value in these war years and which may exert an even more benign influence in the coming years of world recovery and reconstruction.

THE RETIREMENT OF THE SECRETARY OF THE SMITHSONIAN INSTITUTION

THE retirement of Dr. C. G. Abbot as secretary of the Smithsonian Institution has already been announced in SCIENCE. His letter of resignation, dated June 20, addressed to the Board of Regents, reads:

Having occupied the post of secretary of the Smithsonian Institution since February, 1928, and of acting

secretary for one year prior to that, and having passed the age of seventy-two years, I wish to resign from the office, my resignation to take effect as of July 1, 1944.

I feel that it would be quite unfair to the Institution to continue in this responsible position when in the nature of things my capacity must gradually begin to decline. In tendering my resignation I wish to express my gratitude to the board for its kindly and helpful attitude and my desire to be of any service which the board or my successor may feel disposed to suggest.

Dr. Alexander Wetmore, assistant secretary, automatically becomes acting secretary. Dr. Abbot will remain on the staff under the title of research associate.

In resigning the secretaryship Dr. Abbot thanked the members of the staff for their unwavering support and their kindly attitude towards him. He bespoke for his successor and for the institution the continued loyalty and devoted service which had been given so generously during his administration.

SCIENTIFIC NOTES AND NEWS

A PORTRAIT of Dr. Anton J. Carlson, emeritus professor of physiology of the University of Chicago, president of the American Association for the Advancement of Science, was presented to Augustana College, Rock Island, at a recent banquet of the alumni. Dr. Carlson graduated from the college in 1898.

DR. ELMER V. MCCOLLUM, professor of biochemistry at the School of Hygiene and Public Health of the Johns Hopkins University, has been elected a foreign member of the Swedish Academy of Sciences.

DR. HARLOW SHAPLEY, director of the Harvard Observatory, was presented by the Mexican Government with the Order of the Aztec Eagle, third class, at a reception given on July 22 by the Mexican ambassador and Senora de Castillo Najera, in recognition of his cooperation in arranging for the installation of the telescope of the National Astrophysical Observatory at Tonanzintla.

THE University of Oxford will confer an honorary doctorate of science on Dr. Isaiah Bowman, president of the Johns Hopkins University.

THE honorary degree of doctor of science was conferred by the University of Oregon at its sixty-seventh annual commencement on June 4 on Dr. Ralph Works Chaney, professor of paleontology at the University of California. The citation reads: "In recognition of his penetrating researches in paleobotany in general and of the Oregon area in particular; his unique understanding of the historical geology of Western America in relation to that of Asiatic countries; and his deep appreciation of the kinship of science in its broadest aspects and its contribution to the understanding of human values."

WESLEYAN UNIVERSITY at its commencement on June 25 conferred the honorary degree of doctor of science on Dr. Stanley D. Wilson, formerly professor of organic chemistry and dean of the College of Natural Sciences at Yenching University, Peking. Professor Wilson was repatriated on the *Gripsholm* and arrived

in New York in December, 1943. He has been engaged since in research at the California Institute of Technology, and now has been appointed visiting professor of chemistry at Pomona College, where he will take up work on September 1.

THE degree of doctor of laws was conferred at the commencement exercises of the University of Wyoming on Dr. James F. Wilson, professor of animal husbandry at the College of Agriculture at Davis of the University of California.

DR. LELAND W. PARR, professor of bacteriology and head of the department of the School of Medicine of George Washington University, has been elected secretary-treasurer of the Society of American Bacteriologists.

At the annual general meeting of the British Physiological Society held on May 24, the following officers were elected: *President*, Professor E. N. da C. Andrade; *Vice-president*, Sir Edward Appleton; *Honorary Secretaries*, J. H. Awbery (Papers) and Dr. W. Jevons (Business); *Honorary Treasurer*, Dr. C. C. Paterson; *New Members of Council*, Professor S. Chapman, C. H. Collie and Professor H. R. Robinson. At an extraordinary general meeting held on the same day A. F. Joffe was elected an honorary fellow.

THE title of emeritus has been conferred on Dr. Joseph C. Bock, professor of biochemistry at the School of Medicine of Marquette University. He retires after teaching for thirty-two years.

DR. RONALD A. SILOW, formerly assistant geneticist of the Cotton Research Station of the Empire Cotton Growing Corporation, Trinidad, British West Indies, has been appointed visiting professor for the coming year in connection with the Blandy Experimental Farm of the University of Virginia.

DR. WILLIAM WALTER GREULICH, professor of physical anthropology and anatomy and director of the Brush Foundation of the School of Medicine of Western Reserve University, has been appointed professor of anatomy at Stanford University.

DR. J. FISHER STANFIELD, of the State University of Iowa, has been appointed professor of botany and bacteriology and head of the department at Miami University.

DR. MAURICE EWING, now engaged in research for the Navy with the civilian rank of "chief scientist," has been appointed associate professor of geophysics in the department of geology of Columbia University. He will direct graduate instruction in geophysics as part of a postwar program of geological training and research. He also plans to continue his investigations of the continental shelf and the ocean basins.

At the University of Illinois the following members of the faculty have been advanced to full professorships: Dr. Reinhold Baer, mathematics; Dr. R. R. Kudo and Dr. F. B. Adamstone, zoology-physiology; M. K. Fahnestock, mechanical engineering; Dr. L. M. Mott-Smith and Dr. Leland J. Haworth, physics, and Dr. O. T. Bonnett, agronomy.

At Kansas State College, Dr. A. D. Weber has been appointed head of the department of animal husbandry to succeed Dr. C. W. McCampbell, who recently retired to teach and to carry on research work. Dr. James E. Ackert, in addition to his work as dean of the Graduate School, has been made head of the department of zoology. He succeeds Dr. Robert K. Nabours, who will devote his full time to research. Dr. J. H. Burt has retired as head of the department of anatomy and physiology in the School of Veterinary Medicine, but will continue to teach full time. This department has been divided, with Dr. W. M. McLeod as head of the department of anatomy and Dr. E. E. Leasure as head of the department of physiology.

At the University of London, Dr. Frank Horton, professor of physics, has been re-elected vice-chancellor. Dr. H. T. Flint, reader in physics at King's College, has been appointed to the Hildred Carlile chair of physics tenable at Bedford College and Dr. W. N. Bailey, lecturer in mathematics in the University of Manchester, to the university chair of mathematics, also tenable at Bedford College. Dr. S. W. Woolridge, reader in geography at King's College, has been appointed to the chair in geography tenable at Birkbeck College. He succeeds Professor E. G. R. Taylor, who has retired. The title of reader in zoology at University College has been conferred on G. P. Wells.

DR. H. G. SANDERS, lecturer in agriculture at the University of Cambridge, has been appointed professor of agriculture at the University of Reading. He succeeds Professor Robert Rae, who has been appointed agricultural attaché to the British Embassy in Washington.

DR. JOHN R. SWANTON, ethnologist of the Bureau of American Ethnology, has retired after forty-four years' continuous service. At a reception on June 30 his friends and associates took the opportunity to wish him well and many years of happiness. He has been given an honorary appointment as collaborator of the Bureau of American Ethnology. He will live in New England.

DR. DONALD B. KEYES, professor of chemical engineering and head of this division at the University of Illinois, who since 1943 has been chief of the chemical industries branch of the Office of Production, Research and Development of the War Production Board, has been appointed director of the office. He succeeds Dr. Harvey N. Davis, who plans to devote his full time to the presidency of Stevens Institute of Technology.

PROFESSOR VERNON L. FRAMPTON has resigned from the department of plant pathology of Cornell University, to become affiliated with the research division of the National Cotton Council.

DR. ARTHUR P. RICHARDSON, professor and head of the department of pharmacology of the College of Medicine of the University of Tennessee, has been appointed head of the division of pharmacology of the Squibb Institute for Medical Research, New Brunswick. He succeeds Dr. Harry B. Van Dyke, who has become head of the department of pharmacology of the College of Physicians and Surgeons of Columbia University.

DR. OTTO SCHALES, research associate in medicine and tutor in the biochemical sciences at Harvard University, director of the Clinical Laboratories of the Peter Bent Brigham Hospital, has been appointed director of chemical research of the Ochsner Foundation and director of the Biochemical Laboratory at the Ochsner Clinic, New Orleans. The new chemical laboratories of the Ochsner Foundation will specialize in research on the therapeutic aspects of medical enzymology.

P. M. ROXBY, who is retiring from the Rankine chair of geography at the University of Liverpool, which was endowed for him in 1917, will go to Chungking at the invitation of the British Council to be a chief cultural link between China and Great Britain. Professor Roxby has been associated with the department of geography of the university since 1906.

DR. CHARLES HALLILEY KELLAWAY, F.R.S., director of the Walter and Eliza Hall Institute of Research in Pathology and Medicine of the Royal Melbourne Hospital, Australia, has been appointed director of the Wellcome Foundation Research Laboratories in England and in the United States. His headquarters will be in London. Dr. Frank M. Burnet will take charge of the work at Melbourne.

DR. ROBERT REDFIELD, professor of anthropology at the University of Chicago and dean of the Division of the Social Sciences, has leave of absence for six months beginning in September to make a study of social science problems in China. The trip is sponsored jointly by the Social Science Research Council and the University of Chicago. It will be financed by a grant of the Rockefeller Foundation.

DR. VINCENT DU VIGNEAUD, professor of biochemistry at Cornell University Medical College, will deliver on August 1, 3 and 8 the Hitchcock lectures of the University of California at Berkeley. The Hitchcock Foundation, which provides lecturers on "scientific and practical subjects but not for the advantage of any religious sect or upon political subjects" was established in 1872 by Charles M. Hitchcock. A bequest from his daughter, Mrs. Lillie Hitchcock Coit, increased the endowment to \$125,000.

THE annual meetings of the Association of American Geographers and of the National Council of Geography Teachers, that were to have been held from September 10 to 13, have been cancelled.

THE demand for the Smithsonian War Background Studies has been so great that it is no longer possible to continue to print more copies for unrestricted free distribution. The entire cost of the series has been

defrayed from the private funds of the institution and money for a further free edition is not available. The editions of most of the papers have been practically exhausted, and in order that they may continue to be available to those who need them, it has been decided to print additional copies to be sold on a non-profit basis to individuals, other than members of the armed forces. These will be available in August. Hereafter the smaller papers, Nos. 2, 3, 5, 8, 12 and 17, will be sold for 10 cents a copy; all others for 25 cents a copy.

THE Nutrition Foundation has awarded grants to the Harvard Medical School, Boston, to support fellowships in clinical nutrition for the years 1944, 1945 and 1946. The fund will be administered under the supervision of Dr. Frederick J. Stare, assistant professor of biochemistry and nutrition. The fellowships provide for post-doctorate training in medicine and for advanced training in medical nutrition for dietitians.

THE Sealy and Smith Foundation has offered 1 million dollars to the University of Texas for a new general hospital unit at Galveston. The gift is contingent on an appropriation by the university of a second million dollars.

DISCUSSION

EXOTOXINS FROM SLIME MOLDS

LIVING cells exude waste products. This is a well-known physiological function which presents a variety of problems, one of which is the toxic effect of the waste products of one cell upon another. Several years ago I observed the reaction of a slime mold to the exotoxins given off by another slime mold. Publication was delayed in the hope that some information could be had on the organic nature of the exuded waste products. As this has until now proved impossible—it will at best be a difficult task—I have chosen to report briefly the original observation, namely, the reaction of slime molds to one another's exotoxins.

The organism worked upon is the myxomycete, *Physarum polycephalum*, now a familiar source of material for physiological work on protoplasm. The plasmodium, or slime mold is a multinucleate, non-cellular body. The protoplasm of the slime mold *Physarum* is in a continual state of motion, except when dormant. Protoplasmic flow continues in one direction for three quarters of a minute and then reverses. The movement is, in its general appearance,

much like the ebb and flow of the tides. Streaming in the outward direction averages five seconds more than in the return direction: this additional time accounts for the onward progress, the locomotion, of the organism.

Botanists have presumably long known that slime molds rarely recross their tracks. Possibly the cause of this was also suspected to be the toxic nature of the residue left behind by the advancing mold. Not more than this is known of the physiology or the chemistry of the waste products given off by slime molds. The exuded exotoxins may be regarded as secretory products, the whole organism functioning as a kidney. After all, this is true of any living cell. There is an unfortunate tendency in biology and medicine to regard protoplasm in a simple form such as the slime molds represent, as devoid of all the properties of higher organisms, thus forgetting that the properties of the organism as a whole exist in large measure because they are properties of protoplasm. The heart pulsates because protoplasm pulsates. If organisms show irritable response, protoplasm must do likewise. Kidneys secrete because protoplasm secretes.

My casual interest in the exotoxins of slime molds

became an intensive one when, during a study of the fusion of slime molds, certain plasmodia failed to fuse.

Two individual masses of slime mold protoplasm approaching each other will, under favorable conditions, meet and fuse. After uniting, extraordinarily large and well-developed "arteries" of active flow are established at the point of transfusion. The excessive development of the connecting "artery" and the abnormally rapid flow of protoplasm through it are due to the release of pressure in the region of the union. With the sudden release of the surface tension which opposes the outward flow, there is an onrush of protoplasm which augments the rate of streaming and produces over-development of the channel of flow. This phenomenon was the subject of my study. But often, while waiting for fusion, I waited in vain. Two approaching plasmodia would occasionally halt at a short distance from each other, and there remain. A zone of definite width was established and maintained between them.

Another form of the reaction of slime molds against the exotoxins of others of their kind is seen in the direction of movement or locomotion of plasmodia when several are in close proximity to each other. If the time is sufficient to permit waste products to form and collect between the plasmodia, the direction of movement of all of them is away from the center of the group, away from the center of maximum toxicity.

The pertinent facts may be stated as follows. When two slime molds rapidly approach each other and meet head-on, fusion always occurs and is immediate, provided the two plasmodia are of the same species and grown under similar conditions. But if the approach is gradual and there is thus time for the waste products of each plasmodium to collect at the approaching surfaces, then no fusion takes place. In short, no plasmodium will enter the zone of toxic waste products surrounding another plasmodium.

The toxic strip which separates two plasmodia is about 0.15 mm wide. The band is often of extraordinarily constant width which is maintained even when the plasmodia have irregular contours; the two boundaries may fit one into the other very much like two corrugated surfaces in which the crests of one fit into the troughs of the other.

The affinity and antagonism of cells for each other is a problem of great importance, applicable to a variety of situations throughout the living world. The failure of some sperm to accomplish the fertilization of eggs of the same species is due to lack of chemical affinity and this may be a question of exotoxins. Incompatibility due to the presence of exotoxins may also be the cause of the failure of conjugation between protozoa of the same species. "Mating types" in *Paramecia* may be determined by the reactions of

one type to the exotoxins of the other type. The ingestion, or taking in of food, of one unicellular organism by another must in part be determined by the toxicity of the cell which serves as food, and this may be a matter of the environment of waste matter which surrounds the cell ingested. The engulfing of living cells by other cells assumes a special function in phagocytosis. The ingestion of some bacteria and not of others by the scavenger cells of the blood may be a question of the toxic effect of one cell upon another. All these examples, like that of the failure of two slime molds to fuse, may be determined by cellular exotoxins, by the secreted waste products of cells.

WILLIAM SEIFRIZ

UNIVERSITY OF PENNSYLVANIA

CHOLINESTERASES

MENDEL and Rudney, in *SCIENCE* of January 14, 1944, again claimed priority for our earlier¹ discovery of two distinctive types of cholinesterase in the body. Their contention is apparently that since we failed to note a certain similarity of behavior between cholinesterases from blood cells and from serum we could not have been aware of their differences, which were in fact strikingly apparent in our comparisons of the two types of preparations. Even if one accepts their empirical test as definitive, their own data show only 2 per cent. of the activity of human serum to be due to cell type enzyme.

In the same note they quoted de Laubenfels as asserting that we had "thoroughly demonstrated" the existence of the true and pseudo-cholinesterase." This is inaccurate. De Laubenfels² correctly stated that we had proved the existence of two esterases capable of hydrolyzing acetylcholine, without implying that we had proffered a conclusion regarding their relative degree of specificity. Indeed, if we had, our reported evidence would have led us to the opposite conclusion from that of Mendel and Rudney.

We wish to record our support of de Laubenfels'² contention that "pseudo-cholinesterase" is an unfortunate name for an enzyme that has been so long and extensively studied under the name cholinesterase. In addition, current studies of serum cholinesterase in relation to disease, as in myasthenia gravis, as well as the findings of Glick³ on the behavior of the enzyme of the cat superior cervical ganglion, make the acceptance of "pseudo-cholinesterase" as a suitable name for the serum enzyme seem inadvisable.

GORDON A. ALLES

PASADENA, CALIF.

ROLAND C. HAWES

LOS ANGELES, CALIF.

¹ G. A. Alles and R. C. Hawes, *Jour. Biol. Chem.*, 133: 375, 1940.

² M. W. de Laubenfels, *SCIENCE*, 98: 450, 1943.

³ D. Glick, *Jour. Gen. Physiol.*, 21: 431, 1938.

EUBIOTIC MEDICINE

I SHOULD like to submit the term "eubiotic medicine" to take the place of or to supplement the term "preventive medicine." I intend this term to indicate those phases of medical science and of medical service which go beyond the prevention of disease and which foster as well as advance the biologic growth, development and well-being of the individual.

It appears to me that there is no term now current which adequately represents these phases of medicine. The term "preventive medicine" is self-limiting in the adjective preventive. Furthermore, the term "preventive medicine" historically has very distinctive connotation. It represents and embodies a period in the development of medicine which is now definitely past. Its definitive connotations are inherent in the term. They are the very opposite of what is most distinctly characteristic of present-day medicine and what is implied in the proposed term "eubiotic medicine." The eminent proponents of preventive medicine labored in the conviction that the highest competences of medicine were to prevent disease. They definitely believed that it was not possible to directly promote biological well-being. This credo was best stated by Von Behring in the introduction to his "Gesammelte Abhandlungen zur ätiologische Therapie von ansteckenden Krankheiten."¹ He stated:

... For we are of the opinion that in combating diseases we can achieve more by attacking the causes of disease than by an attack on the living cells and organs. ...

Until now we only know that even the best intended, direct attacks on living cells and organs in order to animate or to stimulate them into a state of modified activity, are more likely to harm the cells and organs, than to bestow upon them more health and resistance.

Other terms have been advanced to convey the meanings not expressed by "preventive medicine." One such is "positive health." This term is to say the least barbaric. Some among the English have favored "social medicine," but this term, as was recently pointed out in *The Lancet* of October 30, 1943, page 546 (editorial entitled "Teaching of Preventive Medicine"), encompasses far too many of the economic, industrial and social factors that affect well-being. It is, in other words, vague because it is too embracing.

The elements that enter into the composition of the term "eubiotic medicine" are patent. There are also good precedents for this term in such words as eugenic, euthanasia and euphoria.

IAGO GALDSTON

THE NEW YORK ACADEMY OF MEDICINE

¹ E. Behring, "Gesammelte Abhandlungen zur ätiologischen Therapie von ansteckenden Krankheiten," Leipzig, Georg Thieme, 1893, p. lxx, lxxi.

HANDBOOK ON LABORATORY ANIMALS

THE Universities Federation for Animal Welfare is compiling a handbook on the care and management of laboratory animals. The aim is to provide a concise, practical manual which will facilitate the uniform and humanitarian care of the smaller laboratory animals, and it is in no way intended to produce a comprehensive monograph for each species. It is hoped to publish the work at a price that will make it readily accessible to technicians as well as to scientific workers.

The different chapters deal with (1) animal houses and their pests; (2) the rat; (3) the mouse; (4) the rabbit; (5) the guinea-pig; (6) the vole; (7) the hamster; (8) the cotton rat; (9)¹ the deer-mouse; (10) the ferret; (11) the hedgehog; (12) the pigeon; (13) the fowl; (14) the canary; (15) the frog, the African clawed-toad (*Xenopus laevis*) and certain other amphibia; (16) certain fish; (17) the training of laboratory assistants; (18) the law and practice of animal experimentation, and (19) the use of statistical methods. All chapters are being drafted by individual workers drawn from various laboratories, including the Lister Institute of Preventive Medicine, the London School of Hygiene and Tropical Medicine, the Agricultural Research Council's field station; the Ministry of Agriculture and Fisheries Veterinary Laboratory and also its Fisheries Research Section, the Harper Adams Agricultural College, the Bureau of Animal Population, and various other hospital laboratories and university departments. Collaboration is being received also from the National Institute for Medical Research, the National Veterinary Medical Association and individual workers in many fields. In order to obtain supplementary information, a questionnaire has been forwarded to all workers in Great Britain who hold a license for animal experimentation.²

In present circumstances it is not practicable to draw fully upon American experience, but as general editor of the handbook I should be most grateful for any information which workers in the United States and Canada would forward to me. Reprints, of which two copies would be welcomed, would assist us in our task. The information will be gratefully acknowledged in the text, unless the contrary is requested by those forwarding it. It is hoped that the handbook will be made available both in the United States and in Canada.

ALASTAIR N. WORDEN

INSTITUTE OF ANIMAL PATHOLOGY,
UNIVERSITY OF CAMBRIDGE,
ENGLAND

¹ By Professor Lee R. Dice, University of Michigan.

² The author will be glad to send copies to others on request.

SCIENTIFIC BOOKS

MEDICAL PHYSICS

Medical Physics. Edited by OTTO GLASER. xlv + 1744 pp. The Year Book Publishers, Inc. 1944. \$18.00.

THIS volume represents a comprehensive attempt to describe those aspects of physics which are being utilized in medicine at the present time. There are over two hundred separate articles by contributors who are experienced workers and, in many instances, outstanding authorities in their respective fields. As the editor states, the volume was conceived as "a combination of an *encyclopedia*, sufficiently comprehensive to serve as a reference for all those whose occupations involve any aspect of medical physics; a *textbook*, adequately detailed in exposition to serve students; and a *working instrument*, in which may be found the data necessary for actual application of the principles of physics to medicine."

The subject-matter is too vast to describe or even outline in any detail. A few articles may be named to illustrate the considerable scope of the volume and the wide range of interest. For example, there are detailed sections on such basic subjects as bioelectricity (Beutner), cosmic rays (Wollan), growth (Wetzel), optics (Sheard), photoelectricity (Cashman), spectrographic analysis (Langstroth) and mathematical biophysics (Rashevsky). Of more specific interest are such articles as those on air conditioning and heating, biomechanics, urological methods and various surgical techniques.

The value of the volume is most apparent when it is considered from the viewpoint of the physician who is eager to understand the bases in physics of the phenomena he deals with, or from that of the medical investigator who needs a convenient guide book to physical methods and concise summations of data which are applicable to his work.

The clinician will find instructive material on such subjects as the arterial pulse, audiometers and hearing aids, mechanism of bronchial obstruction, dynamics of cerebrospinal fluid, the circulation, climatic factors in health and disease, electrocardiography, electroencephalography, fever therapy, gastroscopy, work and failure of the heart, roentgenography, photochemistry of vision, etc.

But the volume will prove most useful, if not indispensable, to the medical investigator as a guide to physical methods and data. Thus there are comprehensive sections on biometric methods, the use of isotopes in biological work (together with a table of nuclear properties), photometry, spectrophotometry, centrifugation, cinephotomicrography, endoscopic photography, physical anthropology and other

subjects of similar importance. There are also shorter articles on a variety of specific techniques and on the significance of data obtained by means of these techniques. Among these articles may be mentioned those on the blood cell count, blood volume, electrolyte and water equilibria in the body, electrophoresis, falling drop method, oxidation-reduction potentials, polarimetry, refractometry and volumetric and manometric methods for the measurement of cell respiration and other processes.

There are several features which facilitate use of this volume. The tables of contents are arranged both alphabetically and by medical subjects. Tables of symbols and abbreviations are present in the introduction. Substantial bibliographies are present at the end of each article and enable the reader to follow up his subject in greater detail. The author and subject indices are also very detailed.

There is little in this book which detracts from its general merit. Occasionally, there appears to be misplaced emphasis on subjects which are not strictly within the scope of the volume. For example, there is a rather large section on the chemistry of chlorophyll which, although of considerable interest in itself, does not appear pertinent to the main purpose of the volume. A number of others fall into this group, such as the articles on ecology, on the types of tables used in cystoscopy and on methods used in resuscitation.

In general, the volume appears to have fulfilled the purposes of the editor excellently. Although it is not a text-book in the usual sense, the student of physics or biophysics will find much which he may study intensively, and the medical material will serve to broaden his interests and outlook. For the medical and biological investigator, this volume will undoubtedly prove to be an essential and much used work of reference.

OSCAR BODANSKY

ENZYMES

Enzyme Technology. By HENRY TAUBER. vii + 275 pp. 46 figures. New York: John Wiley and Sons, Inc. London: Chapman and Hall, Ltd. 1943. \$3.50.

ACCORDING to the author, the purpose of this book is designed to present practical information concerning the role and use of enzymes in industry. A large number of subjects have been discussed briefly: Yeast production and utilization; the role of enzymes in brewing; mold fermentation; bacterial fermentation; the production of various enzymes; methods of estimating enzymes; enzymes in the medical field; bread-making and dairy production; the enzymes of meat,

eggs, vegetables, fruits and grains. The use of enzymes in the textile and paper and the wine and dairy industries and other industries where enzymes are employed is given consideration.

There is also a chapter on "Vitamin-destroying Enzymes" and a chapter on "Microbiological Methods for the Estimation of Vitamins."

Many of these subjects are not discussed in sufficient detail, and in some cases the author has not confined himself to the original objectives.

In Chapter VI—"The Production of Enzymes and Methods of Their Estimation"—methods for the preparation of diastatic enzymes from molds, bacteria and pancreas and also proteolytic enzymes are given, whereas the preparation of yeast enzymes, malt diastase and a number of other preparations are described in other chapters. A more reliable index of the contents within the chapter would be helpful to the reader. The only methods included in this chapter cover proteolytic activity, lipolytic activity and a method for saccharogenic amylase activity. Some of the other methods are given in the chapters describing specific enzymes in more detail. It is believed that it would have been helpful to the reader to group the chapters containing material on the amylases, as this procedure would have made possible a more unified treatment of the subject.

The models of Hanes for the structure of the starch molecules are given. It is believed that it is now quite well established that starch consists of straight-chain amylose and the branched-chain amylopectin, consequently the simple Haworth structure does not represent the most recent conceptions of starch structure. The author seems to have confused the starch liquefying property of α -amylase and the as yet unverified amylophosphatase of Waldschmidt-Leitz and Mayer.

The author has brought together a number of recent developments in the less well-known fields, such as the manufacture of leather, pectin, lactic acid and the retting of flax, which will be of interest to the student.

A discussion of the microbiological assay methods for the six B vitamins is given in the last chapter.

The book should prove to be a useful contribution to the growing field of enzyme technology. The scope of the book is rather broad and, consequently, the treatment given each subject is in many cases too brief, but the reader can cover the field more thoroughly by making use of the excellent collection of references given at the end of each chapter.

The printing of the book is satisfactory and the errors are relatively few. The binding is suitable for a book of this type.

CHARLES N. FREY

THE FLEISCHMANN LABORATORIES,
NEW YORK, N. Y.

QUANTUM CHEMISTRY

Quantum Chemistry. By HENRY EYRING, JOHN WALTER and GEORGE E. KIMBALL. 390 pp. New York: John Wiley and Sons. 1944. \$5.00.

"IN so far as quantum mechanics is correct, chemical questions are problems in applied mathematics. In spite of this, chemistry, because of its complexity, will not cease to be in large measure an experimental science, even as for the last three hundred years the laws governing the motions of celestial bodies have been understood without eliminating the need for direct observation." This quotation from the preface expresses well the authors' point of view. The presentation is directed to the graduate student level on the assumption of the standard training in physics, mathematics and chemistry. It is excellent. The material is well arranged and each subject lucidly and thoroughly presented. The number of errors is small for the type of material presented. The reviewer has found about a dozen, of which all are typographical in nature. Separate chapters are devoted to the differential equations involved in ordinary quantum mechanical problems, radiation theory, the general principles and applications of group theory, statistical mechanics and electric and magnetic phenomena. A set of carefully selected references is given in an appendix for each of the major subjects treated. The historical development of the quantum theory is described in the first chapters with a clear tracing of the transition from the "old quantum theory" to the "wave mechanics," authoritative references to classical papers being given. The fundamental postulates of the quantum theory then are stated with no attempt to rationalize away their wonderful mystery. The more difficult points are treated patiently and carefully. The properties of the spin operators and their eigenfunctions are presented only after a thorough treatment of the general angular momentum operators. The rather irritatingly complicated derivation of the second order perturbation equations ordinarily given is alleviated somewhat. It is a pleasure to find group theory in its fundamental and applicable forms treated in a book on beginning quantum mechanics. The same remark applies to the chapter on statistical mechanics. In short any one who masters this book certainly will have gained a good acquaintance with theoretical chemistry and physics.

The book does not fulfil, however, a widely recognized need for a general presentation of the more qualitative aspects of the quantum chemistry. Certain techniques exist and are used generally for applying quantum principles to ordinary problems. In general these center around the Uncertainty Principle and the Correspondence Principle, the first of which is

treated briefly, and the second of which is hardly mentioned. These approaches are generally useful to any one, because the more exact mathematical treatment is so difficult, and they are doubly useful in introducing beginners to the theory. In this respect the

book is insufficient. It may be impossible to accomplish both ends in one volume.

W. F. LIBBY

UNIVERSITY OF CALIFORNIA,
BERKELEY

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE CLEVELAND MEETING

PROGRESS is being made in the preparation of programs for the Cleveland meeting, which will be held from September 11 to 16. Some of the important features and information regarding sessions of a number of sections and societies follow.

Dr. Isaiah Bowman's address as retiring president of the association is scheduled for Monday evening, September 11. Dr. Bowman has returned from his conferences in London and reports that his address has been written.

On Tuesday evening the annual Sigma Xi address will be delivered by Dr. Edwin J. Cohn, of the Harvard Medical School, on "Blood and Blood Derivatives," a subject of the highest medical importance, especially during the war period, to which he has recently made far-reaching contributions.

On Wednesday evening the annual Phi Beta Kappa address will be delivered by Dr. Harlow Shapley, director of the Harvard College Observatory. Dr. Shapley has selected as his subject "A Design for Fighting."

For Thursday evening arrangements have been completed for an illustrated lecture on the National Geographic Society-Smithsonian Institution Archeological Expeditions to Southern Mexico by Dr. Matthew W. Stirling, chief of the Bureau of American Ethnology and leader of the expeditions, and Mrs. Stirling.

Several important symposia are being organized on various phases of international cooperation in science after the war by Dr. Gardner Murphy, professor of psychology in the College of the City of New York; Lawrence K. Frank, chairman of the association's Committee on Science and Society, and Dr. Howard R. Tolley, chief of the Bureau of Agricultural Economics of the Department of Agriculture. Mr. Frank is also organizing a symposium on "Research after the War: The Need for a National Policy on Research."

The Section on Mathematics (A): Sessions on Tuesday afternoon and Wednesday morning for addresses by retiring vice-presidents.

The Section on Chemistry (C): Sessions on Thursday and Friday, mornings and afternoons. Symposia on catalysis and chemotherapy.

The Section on Geology and Geography (E): Sessions each day from Monday through Thursday, mornings and afternoons. A symposium on quartz, sessions on recent

geological research on the Eastern Interior Region, and the retiring vice-presidential address by Dr. M. M. Leighton on "Present Knowledge and Problems Concerning Glacial History of Illinois."

The Section on Zoological Sciences (F): The American Society of Zoologists will meet on Tuesday, Wednesday and Thursday. On Monday the American Society of Parasitologists will hold two sessions for papers and on Tuesday morning a joint session with the American Society of Parasitologists will be devoted to a symposium on "Parasitology in Relation to the War."

The Section on Botanical Sciences (G): The Section will meet on Tuesday afternoon with the session to be devoted to a program of papers by Dr. G. M. Smith, Stanford University, Dr. W. J. Robbins, New York Botanical Garden, and Dr. R. E. Cleland, Indiana University, retiring vice presidents of the Section. Section G will join with the Section on Agriculture (O) on Thursday morning for a session on "Nutrition—Some Current Views," with papers by a microbiologist, a plant breeder and a plant physiologist. The Botanical Society of America and the American Society of Plant Physiologists will hold sessions on Tuesday, Wednesday and Thursday, several of them jointly with other groups. The Mycological Society of America and the Sullivant Moss Society will also hold sessions.

The Naturalists' symposium on "Biology and Human Progress" will be held on Thursday afternoon. The Ecological Society of America will meet from Tuesday to Thursday. A joint session with the Section on Education (Q) on Wednesday morning will be devoted to a symposium on "The Teaching of Ecology" and "Ecology in General Courses in Biological Science." The Genetics Society will meet Tuesday through Thursday for invitation papers and demonstration papers, and will hold joint sessions with the American Statistical Society, the American Society of Zoologists and the American Society of Naturalists. On Friday and Saturday the National Association of Biology Teachers will hold business meetings and sessions for invited papers.

The Section on Anthropology (H): Sessions on Friday morning and afternoon and Saturday morning.

The Section on Psychology (I): The section will join with the American Psychological Association and the American Association for Applied Psychology on Monday and Tuesday for sessions that will be devoted almost wholly to organization problems. Section I will hold a joint session with the Section on Education (Q) on Tuesday evening.

The Section on Social and Economic Sciences (K): A session is being arranged to include the address of the retiring vice-president. The Biometrics Section of the American Statistical Association will hold sessions Monday through Thursday, including joint sessions with the American Society for Horticultural Science, the Genetics Society of America, the Econometric Society and the Section on Historical and Philological Sciences.

The Section on Historical and Philological Sciences (L): One of the features of the program of Section L will be a symposium on "Trends in Scientific Research." This session will be held on Wednesday afternoon. Three other sessions are planned.

The Section on Engineering (M): Sessions on Tuesday and Wednesday. The retiring vice-president, Dr. Thorndike Saville, will deliver his address at a luncheon at the Cleveland Engineering Society.

The Section on Medical Sciences (N): The Section is planning sessions for Monday, Tuesday and Wednesday. The Sub-section on Dentistry will hold a symposium on "Dental Caries and Fluorine" on Monday.

The Section on Agriculture (O): On Thursday morning Section O will join with Section G for a symposium on "Nutrition—Some Current Views." Papers will be read by Dr. R. E. Buchanan, Dr. R. J. Garber and Dr. A. E. Murneek. The American Society for Horticultural Science will meet on Tuesday, Wednesday and Thursday.

The Section on Education (Q): Section Q and Section I will meet jointly on Tuesday evening. The section also will hold a joint session with the Ecological Society of America for a symposium on the teaching of ecology.

The National Association of Science Writers is proposing a symposium on the role of the daily newspaper on the development of science in the United States.

On Tuesday and Wednesday, the Research Council on Problems of Alcohol will hold a symposium on alcoholism. The council will conduct part of its program in collaboration with the Cleveland Committee on Alcoholics, the chairman of which is Judge Lewis Drucker.

SOCIETIES AND ACADEMIES

THE ANNUAL MEETING OF THE ROYAL SOCIETY OF CANADA

THE 1944 meeting of the Royal Society of Canada was held at the University of Montreal from May 29 to 31. New fellows were presented at the first general meeting. Those elected to the scientific sections were as follows:

Section III (Chemical, mathematical and physical sciences): R. C. Dearle, G. S. Field, John T. Henderson, G. deB. Robinson, W. Ure.

Section IV (Geological sciences): J. W. Ambrose, G. V. Douglas, H. B. Yates.

Section V (Biological sciences): J. A. Anderson, W. V. Cone, G. E. Hall, W. F. Hanna, Georges Maheux, D. S. Rawson.

Lieutenant General A. G. L. McNaughton, who had been elected an honorary fellow in 1941, while he was absent from the Dominion as Commander in Chief of Canada's Army Overseas, was presented at this meeting.

The society's medals were presented at the evening meeting on May 29, as follows: The Flavell Medal to Professor Velyien E. Henderson, of the University of Toronto, in recognition of contributions to knowledge in the fields of pharmacology, physiology and therapeutics, including the discovery of the anesthetic properties of cyclopropane; the Henry Marshall Tory Medal to Professor Frank Allen, of the University of Manitoba, for his contributions to the subjects of optics and acoustics and especially to a border region of physics and physiology; the Tyrrell Medal to Professor Harold A. Innis, of the University of Toronto.

Following the presentation of the medals, the presi-

dent of the society, Mgr. Olivier Marault, rector of the University of Montreal, delivered his presidential address "Montréal—une synthèse." The popular lecture on "War, Peace and Commerce" was given on the evening of May 30 by Dr. B. K. Sandwell.

In Section III, the presidential address was delivered by Professor Thorvaldson, who spoke on "The Solid State," reviewing the various theories of chemical reactions in the solid state and the experimental evidence in support of them. This was followed by a symposium on the same subject, in which Professor M. A. Peacock described the methods of identification of solid phases by crystallographic means and Professor E. F. Burton showed some recent photographs taken with the Toronto electron microscope of the forms of solid particles of ultra-microscopic dimensions. The final paper of this symposium was on rubber by Dr. G. S. Whitby, who described the chemical constitution and related physical properties of several of the new artificial rubbers now being produced.

Among the thirty-two other papers presented to the section, mention may be made of one by Professor Frank Allen, in which results of experiments on the sensitivity of the color sensations were described. He finds that when the right eye, for example, is adapted to red light, the red sensation is reduced, but in the left eye all three sensations (red, green and violet) are enhanced. If the eye is rested after adaptation for three minutes, a reversal in sensitivity occurs. There is thus an oscillation of sensitivity. A paper on further simplification in thermodynamical calculations along lines previously developed was read by Profes-

sor A. N. Shaw. Dr. J. A. Pearce and E. C. Walker reported the orbital elements of Lambda Andromedae based on a series of measurements made on high dispersion spectrograms taken at Victoria. Dr. E. C. Beals discussed results which indicate that some new molecular absorption lines recently discovered show characteristics closely similar to atomic lines. It is suggested that their probable origin is to be found in the solid particles responsible for general absorption in interstellar space and that laboratory investigations of the absorption spectra of such particles as are likely to be present in interstellar space might be fruitful in their identification. A new mechanical height computer for radiosonde observations was described and shown by Dr. W. E. Knowles Middleton.

In Section IV, Dr. W. A. Bell's presidential address dealt with the use of some floras in Canadian stratigraphy. Fossil floras have proved very useful in subdividing the very thick Carboniferous sediments of the Maritime Provinces into six groups, of which three are Mississippian and three Pennsylvanian. The use of the terms Mississippian and Pennsylvanian is more appropriate as regards major floral and tectonic events of the Acadian province than Lower and Upper Carboniferous. The former terms are not synonymous with the latter, for the Mississippian terminated in an early part of Upper Carboniferous time, as in the Mississippian valley region. The group subdivision, established mainly on floral evidence, is apparently the most natural one, for it is corroborated by tectonic events. Coal formation was not confined to one age as formerly assumed, but took place locally in the Pennsylvanian in each of the three ages represented by the groups of strata.

In Western Canada stratigraphic work of Dr. F. H. McLearn made possible the recognition of a sequence of three fossil floras in the Lower Cretaceous, respectively of Barremian (and? Neocomian), Aptian and Albion ages. Coals were deposited in Barremian time in southern Alberta and the Yukon, in Aptian time in northern Alberta and central British Columbia.

Nineteen other papers on geological and mineralogical researches were presented. Dr. Madeleine Fritz, of the Royal Ontario Museum of Paleontology, reported the recent discovery of the bryozoan species

Trachytoechus moniliformis Fritz, n. sp., in the Gaspé sandstone of Lemieux Township, Gaspé County, in the interior of the Gaspé peninsula. This has provided evidence to substantiate the belief that the rocks in which the specimen was found are of Middle Devonian age. Dr. F. J. Alcock, of the Geological Survey, Ottawa, presented evidence based on the findings of several striated surfaces and many erratics in central Gaspé which support his already published conclusions that the Labrador ice sheet crossed the Shick-shock Mountains.

Dr. H. S. Jackson, of the University of Toronto, president of Section V, spoke on "Life Cycles and Phylogeny in the Higher Fungi." The discussion centered in a comparison of life cycles in the rusts with those in the red algae. It was shown that not only do the normal cycles correspond very closely but that the same sort of simplified cycles occur in both groups. A life cycle comparable to that of the ascomycetes also occurs among the simplified red algae.

Professor Velyien Henderson, the Flavelle Medal winner, presented an invitation paper entitled "Studies in Anesthesia with the Cyclopropane Group." Professor A. T. Cameron, of the University of Manitoba, outlined the results of his researches on the relative sweetness of certain sugars and mixtures of sugar. If a solution contains known concentrations of two or more sugars, a means has been found for calculating the sweetness of this mixture in terms of that of a specific concentration of sucrose or of glucose. It has been demonstrated that the sweetness of 25 per cent. sucrose is not more than (and is probably less than) 3.3 times that of 5 per cent. sucrose.

Forty-three other papers on various phases of biological and medical sciences made up the program of Section V.

Officers elected for the coming year were: *President*, Professor J. K. Robertson, Queens University, Kingston; *Vice-president*, Professor E. S. Moore, University of Toronto; *President of Section III*, Dr. J. A. Pearce, Dominion Astrophysical Laboratory, Victoria, B. C.; *President of Section IV*, Dr. J. S. DeLury, University of Manitoba; *President of Section V*, Dr. Robert Newton, president of the University of Alberta.

J. R. DYMOND

SPECIAL ARTICLES

EXTRINSIC FACTOR IN PERNICIOUS ANEMIA: INEFFECTIVENESS OF PURIFIED CASEIN AND OF IDENTIFIED COMPONENTS OF THE VITAMIN B COMPLEX^{1,2}

WHEN beef muscle together with normal human gastric juice is administered daily to suitable patients

¹ From the Thorndike Memorial Laboratory, Second and

with Addisonian pernicious anemia, a hematopoietic response appears within 10 days.³ Like beef muscle, several sources of the vitamin B complex, such as milk,⁴ eggs,^{5,6} liver,⁷ yeast,⁸ rice polishings and wheat germ,⁹ contain the so-called extrinsic factor for the

Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Mass.

hematopoietic reaction with normal human gastric juice (intrinsic factor). Observations yet to be published indicate that the active material can be removed from beef muscle by repeated extraction with dilute acetic acid and that it is resistant to autoclaving and to alkalization. Likewise, as shown below, extrinsic factor can be partially or completely removed from crude casein by repeated precipitation or by extraction with dilute acid or with alcohol. Such procedures tend also to remove the known members of the vitamin B complex.

The lack of potency as extrinsic factor of riboflavin¹⁰ and nicotinic acid¹¹ has already been reported. In the present study it was proposed to test additively the extrinsic factor activity of all members of the

Observations were made on a series of ten patients with typical Addisonian pernicious anemia. A full description has been given elsewhere¹³ of the hematological methods and the interpretation of results, especially of reticulocyte responses,¹⁴ as well as of the restrictions on the character and hours of administration of the basal diet. The various types of casein and certain of the vitamins tested were kept in dry form until just before being given to the patient. Biotin was dissolved in 30 per cent. alcohol, and choline hydrochloride, xanthopterin and folic acid in small amounts of water. These and the folic acid concentrate employed in Case 100 were kept in the ice-box as separate solutions until immediately before use.

The results shown in Table 1 apparently demon-

TABLE 1

EFFECT OF DAILY ADMINISTRATION OF VARIOUS TYPES OF CASEIN TOGETHER WITH 150 CC OF NEUTRALIZED NORMAL HUMAN GASTRIC JUICE DURING A 10-DAY PERIOD

Type of casein	Case 91	Case 92	Case 93	Case 94	Case 95
	grams daily				
"Washed" (A. H. Thomas)	50	50	50	50	50
"Water soluble vitamin-free" (Harris)*
Alcohol extracted†	50
Initial R.B.C. (mils./cu.mm.)	1.53	2.56	1.07	1.44	1.88
Reticulocyte peak (per cent.)	15.0	7.5	10.8	5.6	2.4
Interpretation	pos.	pos.	pos.	weak pos.	neg. ‡

* Exhaustively extracted with dilute acids during manufacture.

† "Washed casein" (A. H. Thomas) was extracted with cold 65 per cent. alcohol five times, then once with hot 95 per cent. alcohol.

‡ In a second 10-day period during which 30 grams of Ventriculin N.N.R. were administered daily, this patient showed a reticulocyte response reaching a peak of 24.8 per cent. from an initial red blood cell level of 1.34 mils./cu.mm.

vitamin B complex and of certain other accessory nutritional factors as they became available in pure form.¹² It was planned to administer simultaneously casein rendered free of extrinsic factor, on the theoretical basis that one or more of the vitamins, even if not effective independently, might become active as a prosthetic group on the casein molecule as a result of the action of the gastric juice.

strate that the daily administration of 50 grams of A. H. Thomas "washed casein" (Cases 91 and 92), or of Harris "water-soluble vitamin-free casein" (Cases 93 and 94), simultaneously with 150 cc of normal human gastric juice gave rise to moderately positive hematopoietic effects. However, after A. H. Thomas "washed casein" was extracted five times with cold 65 per cent. alcohol and once with boiling 95 per cent. alcohol, it no longer possessed extrinsic factor activity (Case 95). Borden "Labco vitamin-free casein" (Table 2, Cases 99 and 100) was also found to be ineffective. The hematopoietic activity noted when one of the pure vitamin mixtures was given in combination with Harris "water soluble vitamin-free casein" (Table 2, Case 98) resembles that seen fol-

results of certain tests for extrinsic factor activity in pernicious anemia which have been made by other investigators: A. D. Welch, C. V. Moore and L. D. Wright: Xanthopterin, folic acid concentrate and "known crystalline B vitamins except folic acid." R. W. Vilter and T. D. Spies: Inositol, folic acid concentrate, pyridoxine and adenylic acid.

¹³ W. B. Castle and T. H. Ham, *Jour. Am. Med. Assn.*, 107: 1456-1463, 1936.

¹⁴ G. R. Minot and W. B. Castle, *Lancet*, 2: 319-330, 1935.

² The expenses of this investigation were defrayed in part by the J. K. Lilly gift to the Harvard Medical School.

³ W. B. Castle and W. C. Townsend, *Am. Jour. Med. Sci.*, 178: 764-777, 1929.

⁴ F. R. Miller and W. H. Pritchard, *Proc. Soc. Exp. Biol. and Med.*, 37: 149-152, 1937.

⁵ K. Singer, *Wien. klin. Wchnschr.*, 45: 1063-1064, 1932.

⁶ D. K. Miller and C. P. Rhoads, *New Eng. Jour. Med.*, 211: 921-924, 1934.

⁷ F. Reimann, *Med. Klin.*, 1: 880-881, 1931.

⁸ M. B. Strauss and W. B. Castle, *New Eng. Jour. Med.*, 207: 55-59, 1932.

⁹ W. B. Castle, *Ann. Int. Med.*, 7: 2-5, 1933.

¹⁰ F. Diehl and J. Kühnau, *Deutsches Arch. f. klin. Med.*, 176: 149-153, 1934.

¹¹ C. Faarup and A. S. Ohlsen, *Ugesk. f. laeger*, 102: 905-906, 1940.

¹² Since the completion of the present observations we have learned by personal communications of the negative

TABLE 2
EFFECT OF DAILY ADMINISTRATION OF VARIOUS SUBSTANCES TOGETHER WITH 150 CC OF NEUTRALIZED NORMAL HUMAN GASTRIC JUICE

Substances	Case 96	Case 97	Case 98	Case 99	Case 100
<i>First Period—10 Days</i>					
<i>Casein</i>					
"Water soluble vitamin-free" (Harris)*			50
Alcohol extracted†	50	50
"Vitamin free—Labco" (Borden)‡	50	50
<i>Accessory Factors§</i>					
Thiamin	0.1	0.1	0.1	0.1	0.1
Riboflavin	0.1	0.025	0.025	0.1	0.1
Niacinamide	0.1	0.1	0.2	0.2	0.2
Pyridoxine hydrochloride	0.1	0.1	0.1	0.1	0.1
d-Calcium pantothenate	..	0.1	0.1	0.1	0.1
p-Aminobenzoic acid	2.0	2.0	2.0
Choline hydrochloride	0.3	0.3	0.3
i-Inositol	0.2	0.2	0.2
Biotin	0.002	0.002
Xanthopterin	0.009	0.005
Folic acid	0.0036	0.0023
Initial R.B.C. (mils./cu.mm.)	1.56	1.79	1.73	1.17	1.50
Reticulocyte peak (per cent.)	1.4	2.2	6.4	1.9	1.0
Interpretation	neg.	neg.	pos.	neg.	neg.
<i>Second Period—10 Days</i>					
<i>Beef muscle</i>				200	
Meat extract¶	35 cc.
Ventriculin N.N.R. (without gastric juice)	30	30	30
Initial R.B.C. (mils./cu.mm.)	1.66	1.56	1.80	1.54	1.79
Reticulocyte peak (per cent.)	17.2	11.2	7.4	13.6	8.9
Interpretation	pos.	pos.	second pos.	pos.	pos.

* Exhaustively extracted with dilute acids during manufacture.

† "Washed casein" (A. H. Thomas) was extracted with cold 65 per cent. alcohol five times, then once with hot 95 per cent. alcohol.

‡ Repeated isoelectric precipitation in progressively more dilute solutions of sodium chloride during manufacture.

§ Folic acid and folic acid concentrate (Case 100), both prepared by fermentation methods, and xanthopterin were obtained through the courtesy of Dr. Y. Subbarow, Lederle Laboratories, Pearl River, N. Y.; other accessory factors (except p-aminobenzoic acid) through the courtesy of Dr. D. F. Robertson, Merck and Company, Rahway, N. J.

¶ Courtesy of Mr. Braxton Valentine, Valentine's Meat-Juice Company, Richmond, Va. (35 cc are derived from 600 grams of lean beef).

lowing administration of this type of casein alone (Table 1, Cases 93 and 94). This positive effect is, therefore, probably attributable to the impurity of the casein. The pure vitamin mixtures were inactive when administered in combination with other types of casein (Table 2, Cases 96, 97, 99 and 100).

These observations suggest: (1) that the careful purification required to render crude casein "vitamin free" is also essential for the elimination of the extrinsic factor; (2) that a combination of casein so extracted with the pure accessory factors used and in the dosage indicated did not reconstitute the extrinsic factor activity of the crude casein; and (3) that, nevertheless, it is reasonable to continue to regard the extrinsic factor as a thermostable component of the vitamin B complex as yet unidentified.^{8,15}

W. B. CASTLE

JOHN B. ROSS

CHARLES S. DAVIDSON

JOSEPH H. BURCHENAL

HERBERT J. FOX

THOMAS HALE HAM

PHOTOSENSITIVITY AS A CAUSE OF FALSELY POSITIVE CEPHALIN- CHOLESTEROL FLOCCULA- TION TESTS¹

THE cephalin-cholesterol flocculation test has been proposed by Hanger² as a method of detecting active hepatic disease. Others^{3,4,5} have reported that normal individuals showed positive reactions of varying degree and frequency. Our use of this test has also been complicated by the frequent yet irregular occurrence of falsely positive reactions of the 2 and 3 plus grade. A puzzling feature was the fact that sera giving falsely positive reactions in one laboratory consistently gave negative reactions when tested in a

¹ This investigation was conducted under the Commission on Measles and Mumps, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, U. S. Army, Washington, D. C. The studies were done at the Medical Clinic, Hospital of the University of Pennsylvania, and at the Biochemical Laboratory, Philadelphia General Hospital.

² F. M. Hanger, *Jour. Clin. Investigation*, 18: 261, 1939.

³ F. J. Pohle and J. K. Stewart, *Jour. Clin. Investigation*, 20: 241, 1941.

⁴ J. G. Mateer, J. I. Baltz, P. F. Marion and J. M. MacMillan, *Jour. Am. Med. Assn.*, 121: 723, 1943, Postscript.

⁵ J. W. Oliphant, A. G. Gilliam and C. L. Larson, *Pub. Health Rep.*, 58: 1233, 1943.

¹⁵ R. R. Williams and T. D. Spies, "Vitamin B₁ (Thiamin) and Its Use in Medicine," p. 134. New York: Macmillan Company, 1938.

different laboratory. This discrepancy occurred even when the same technician, using the same reagents and glassware, performed the tests in the two laboratories. During the winter months, the differences were not great, but with the advent of spring and summer, they became progressively more accentuated. Attempts to relate this to improper cleansing of glassware, impurities in reagents, differences in sensitivity of the antigen and details of manipulation failed to provide more than a partial explanation. It was then noted that the two laboratories differed markedly with respect to illumination and that the falsely positive reactions always occurred in the one which was well lighted by several large windows. The other laboratory, in which satisfactory results were usually obtained, was poorly lighted.

In order to study the effect of light on this reaction, a number of experiments of the following type were carried out: Fresh serum was obtained from normal subjects who had no detectable evidence of liver disease and also from subjects with known liver disease. Duplicate preparations of each serum with saline and antigen were then made according to the technique of Hanger.² The Difco cephalin-cholesterol antigen was used. One set was placed before a window so that the preparations would be exposed to daylight. The duplicate set was placed in a dark cabinet. Readings were made after 24 and 48 hours. This procedure was carried out at both laboratories previously described, and also at a third laboratory in a different city.

The results in all three laboratories were nearly identical. Table 1 shows representative results of such experiments. When the serum-saline-antigen mixtures were protected from light, none of the 13 normal sera produced flocculation. The results with the duplicate set, which had not been protected from light, were strikingly different. In these, positive reactions, 1 to 4 plus, were obtained in 9 of the 13 after 24 hours, and in all after 48 hours. A similar effect was obtained with exposure to the bright light of an ordinary incandescent filament lamp. None of the men in this group presented evidence of liver disease detectable by physical examination or by application of a group of liver function tests. Thus, the positive reactions obtained in the exposed tubes were false.

The tests on sera from the patients with known liver disease prove that protection from light does not prevent the truly positive reactions. All showed positive reactions of varying degree in the tubes protected from light, and in 2 the flocculation was maximal (Table 1). However, the degree of flocculation given by 4 of the 6 pathological sera was greater when the serum-antigen mixtures were exposed

TABLE 1
EFFECT OF ILLUMINATION ON RESPONSE OF THE CEPHALIN-CHOLESTEROL FLOCCULATION TEST

Case No. or Initial	Protected from light		Exposed to light		Remarks
	24 hrs.	48 hrs.	24 hrs.	48 hrs.	
12	0	0	0	1+	Normal
"	0	0	3+	1+	3 days later
"	0	0	0	1+	12 days later
16	0	0	1+	1+	Normal
"	0	0	0	2+	15 days later
15	0	0	3+	3+	Normal
"	0	0	4+	4+	6 days later
"	0	0	3+	3+	15 days later
9	0	0	2+	3+	Normal
11	0	0	2+	3+	Normal
14	0	0	3+	3+	Normal
6	0	0	0	1+	Normal
13	0	0	3+	3+	Normal
8	1+	1+	2+	3+	Subsiding hepatitis
5	0	1+	3+	4+	Subsiding hepatitis
T.G.	1+	1+	4+	4+	? liver abscess
W.	1+	2+	4+	4+	Chronic extra-hepatic obstruction
G.	4+	4+	4+	4+	Hepatitis and pneumonia
S.	4+	4+	4+	4+	Biliary cirrhosis

to light. The other 2 showed maximal flocculation under both conditions of illumination.

It was also noted that the results varied with the location of the test preparations in any one laboratory, the number of falsely positive tests being directly related to the intensity of illumination. The reactions in subdued light and total darkness were usually the same.

The evidence that the reaction is photosensitive seems unquestionable.⁶ It has been previously observed that the sensitivity of the cephalin-cholesterol antigen is influenced by the extent to which it is exposed to light in the course of "ripening."³ Presumably due to this difference in sensitivity of various antigens, which even seems to involve vials with the same lot number purchased at the same time, some discrepancies in results have been obtained. However, the influence of light on the reaction itself appears to be a more frequent source of variable results, and this factor apparently has not been previously recognized.

In addition to the effect of light on the serum-saline-antigen mixtures, preliminary studies have suggested that the following other factors may influence the cephalin flocculation procedure: (1) serum diluted and allowed to stand for 5 hours, before mixing with the antigen, resulted in falsely positive reactions whether exposed to light or kept in the dark. The number of falsely positive tests and the degree of flocculation was increased, however, if the diluted serum, alone, was exposed to light before mixing with the antigen. (2) Flocculation generally occurred more rapidly and completely at 37.5° C. than at room temperature. Positive results frequently have been ob-

⁶ The possibility that light may influence other flocculation procedures deserves investigation.

tained at 37.5° C. when the response was negative at room temperature.

The need for standardization of the conditions under which the cephalin flocculation procedure is carried out is obvious. This is especially important in connection with the use of this test in various geographical locations, in which widely differing conditions, in respect to light and temperature, may be encountered. The most satisfactory results have been obtained when the reagents and sera were protected from prolonged exposure to bright light, and when the antigen was added soon after the serum was diluted with saline. It is not yet possible to define the ideal temperature conditions for this reaction, but it appears that more reliable results are obtained at 20 to 25° C. than at 37.5 degrees. Variable results due to differences in sensitivity of the antigen can be partially eliminated by the frequent inclusion of normal control samples. Work is continuing in an attempt to define more exactly the conditions that will yield the most dependable results. However, the procedure is even now capable of providing useful information when performed under the conditions described above.

SUMMARY

(1) Flocculation of cephalin-cholesterol emulsions by blood serum is markedly influenced by the amount of light to which the serum-saline-antigen suspensions are exposed. Protection from bright light, natural and artificial, has eliminated many falsely positive reactions. (2) Other factors that appear to influence the cephalin flocculation procedure have been briefly mentioned. Misses Dorothy Feinberg, Arvilla Howley and Mary Lanning contributed helpful technical assistance.

JOHN R. NEEFE,
Captain, M.C., A.U.S.

JOHN G. REINHOLD

A RHODOTORULA DEFICIENT FOR PARA-AMINO-BENZOIC ACID

In November, 1943, Mr. Manfred Wahl of Philadelphia furnished us with a pink yeast which he had isolated and cultivated from a development in an old culture of beer yeast which Mr. Wahl had attempted to rejuvenate with other dormant cultures. Through the courtesy of Dr. Lynferd J. Wickerham, associate zymologist, Fermentation Division, Northern Regional Research Laboratory, Peoria, Ill., it was identified as a strain of *Rhodotorula aurantiaca* (Saito) Lodder. Preliminary experiments showed that this yeast grew well at 25° C on a basal medium composed of KH_2PO_4 , MgSO_4 , asparagine and dextrose solidified with purified agar and supplemented with thiamine and peptone. When peptone was omitted the growth in the first transfer was scanty, and subcultures on the

same medium failed completely. It appeared probable that this strain of *R. aurantiaca* suffered from growth-substance deficiencies which were not corrected by the addition of thiamine to the basal medium but were satisfied by the substances supplied by peptone.

Yeasts with complete or partial deficiencies for thiamine, biotin, *i*-inositol, pyridoxine and pantothenic acid have been described. However, we were unable to induce the growth of *R. aurantiaca* by the addition of a mixture of these 5 substances to our basal medium. Excellent growth was obtained when the basal agar medium was supplemented with a mixture of para-amino-benzoic acid, calcium pantothenate, guanine, hypoxanthine, *i*-inositol, nicotinamide, pyridoxine, pimelic acid, riboflavin, thiamine, biotin methyl-ester and 2-methyl-1, 4-naphthohydroquinone diacetate. In fact, the growth was more vigorous and the color a deeper red on the medium supplemented with the pure growth substances than on the peptone medium (containing 8 mg of neopeptone per tube). Good growth was obtained also on a medium prepared by adding 5 per cent. of desiccated malt extract to 1.5 per cent. Difco agar, but the color was a deep dull red instead of the bright red observed on the medium supplemented with the mixture of growth substances.

In order to determine the effective substances the basal agar medium was supplemented with 11 of the growth substances mentioned above, one being omitted. Growth was scant when thiamine or para-amino-benzoic acid was omitted; it was unaffected by the omission of any one of the other ten. It appeared, therefore, that *R. aurantiaca* suffered from a complete deficiency for these two growth substances. Further experiments confirmed this finding. The yeast grew well on the basal medium prepared with purified agar supplemented with thiamine and para-amino-benzoic acid. It did not grow on the same medium to which thiamine alone or PAB alone was added. It required molecular thiamine, as no growth was obtained when thiamine was replaced by the thiazole or pyrimidine intermediates of thiamine singly or together. The intensity of the pink color was related to the supply of PAB. In media with less than an optimum quantity of PAB the color was paler and tended toward orange as compared to the deeper pink which developed when more PAB was supplied.

The yeast was grown at 25° in test-tubes containing 5 ml of the basal solution and 10 μ moles of thiamine per tube plus various amounts of PAB. Turbidity measurements were made after 48, 72, 96 and 149 hours incubation. Under these conditions a positive effect of 0.001 μ mole of PAB (0.000137 μ g) was observed after 72 hours. Growth increased with

the amount of PAB up to 0.1 μ mole; it was approximately the same with 0.1, 0.5 and 1.0 μ mole. Somewhat less growth was obtained with 10 μ moles of PAB than with 1 μ mole.

Schopfer¹ reported that *R. aurantiaca* grew poorly in a mineral-dextrose solution containing asparagine. The addition of thiamine doubled growth, but it was still poor. The addition of pyrimidine, thiazole or thiochrome was ineffective. Schopfer's results as far as they go agree substantially with ours.

We concluded that our strain of *R. aurantiaca* suffers from a complete deficiency for thiamine and for PAB. Its sensitivity to PAB appears to be of the

same order of magnitude as that of some other organisms to biotin. Its growth on media supplemented with peptone or malt extract demonstrates the presence of PAB (or a substitute therefor) in those natural substances. *R. aurantiaca* might be useful for the microbiological assay of PAB or of molecular thiamine and for the study of the function of PAB and its relation to the sulfa drugs.

WILLIAM J. ROBBINS
ROBERTA MA

NEW YORK BOTANICAL GARDEN
AND DEPARTMENT OF BOTANY,
COLUMBIA UNIVERSITY

SCIENTIFIC APPARATUS AND LABORATORY METHODS

ATTACHING POINTERS TO MICROSCOPE SLIDES

In preparing practical slide examinations in such subjects as vertebrate embryology or histology, it is frequently necessary to direct the student to a particular detail selected from many others present in a preparation. Various methods for solving this problem are in use in different teaching laboratories; e.g., (1) accompanying the slide with a mimeographed sketch on which various selected details may be indicated by name or number; (2) covering all extraneous matter with gummed paper, leaving exposed only the detail to be observed by the student; (3) pasting paper pointers to cover slips; (4) using ocular pointers; (5) ringing cover slips with diamond point object markers fitting into the nosepiece of a microscope. It is unnecessary to point out decided disadvantages inherent in each of the methods mentioned above.

Since our difficulties with this problem must be paralleled in many other laboratories, it may be of general interest to describe here a technique which we find to be very satisfactory. Using very sharp scissors, small pointers, in the form of isosceles triangles, are cut from thin, tinted Cellophane. Pointers cut from a good quality of bond paper are often good enough, but under a magnification of 300 or 400 diameters such paper pointers look quite ragged.

The pointers are glued to clean cover slips with thin clarite, balsam or damar, and the cover slips dried on a warming stage. Sections fresh from xylene are mounted in clarite (60 per cent. by weight in toluene) under such cover slips, with the pointer between the section and the cover. By gentle manipulation of the cover slip under a dissecting or compound microscope, it is easy to place the tip of the pointer in any position desired. We have not been troubled by having pointers move during the drying process. After the preparation has been thoroughly dried (e.g., one month at 50° C.), there is no further danger of moving or blunting the pointer. The slide

then constitutes a permanent item in a practical examination set.

HADLEY KIRKMAN
JEAN ALLEN KOGAN

DEPARTMENT OF ANATOMY,
STANFORD UNIVERSITY SCHOOL OF MEDICINE

LOAN TEACHING SETS ON BACILLARY DYSENTERY

THERE are now available for teaching purposes six sets, each consisting of eighty-six 28 × 40 mm slides, thirty-five in Kodachrome, and a condensed lecture brochure. These slides cover the subject of acute and chronic bacillary dysentery, including the newer aspects of the epidemiology, pathology, bacteriology, serology, clinical phases, prophylactic and curative therapy. They are available on loan to Army, Navy, public health and university teachers without cost except that of mailing. The project is part of a long-range plan of the Dysentery Registry for the dissemination of our ever-growing knowledge of the important subjects of bacillary dysentery, enteritis and colitis. It was deemed expedient to stress the military aspects at this time. Requests will be honored in order of their receipt. The date on which the slides will be used should be specified. The total time of presentation is approximately 90 minutes at the ordinary talking speed. The slides are so arranged that they may be presented in a single lecture, two lectures of 45 minutes each or three lectures of 30 minutes each.

JOSEPH FELSEN

THE DYSENTERY REGISTRY,
THE BRONX HOSPITAL,
NEW YORK 56, N. Y.

BOOKS RECEIVED

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¹ W. H. Schopfer, *Protoplasma*, 31: 105-135, 1938.